FILE 'CAPLUS, USPATFULL, BIOTECHNO, IPA, BIOSIS, EMBASE, TOXCENTER, MEDLINE, CANCERLIT, DRUGU' ENTERED AT 11:29:36 ON 02 SEP 2004

L1 16 S BONE MATASTAS?
L2 32986 S BONE METASTAS?
L3 6483 S ENDOTHELIN A RECEPTOR
L4 58968 S ENDOTHELIN-1
L5 61364 S L3 OR L4
L6 99 S L2 AND L5
L7 60 DUPLICATE REMOVE L6 (39 DUPLICATES REMOVED)
L8 10 S L7 AND PY<=2000

=> d 1-10 bib abs

L8 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:788871 CAPLUS
DN 123:189302
TI Identification of **endothelin-1** in the pathophysiology of metastatic adenocarcinoma of the prostate
AU Nelson, Joel B.; Hedican, Sean P.; George, Daniel J.; Reddi, A. H.; Piantadosi, Steven; Eisenberger, Mario A.; Simons, Jonathan W.
CS James Buchanan Brady Urological Inst., Johns Hopkins Hosp., Baltimore, MD, 21287-2411, USA
SO Nature Medicine (New York) (**1995**), 1(9), 944-9
CODEN: NAMEFI; ISSN: 1078-8956
PB Nature Publishing Co.
DT Journal
LA English
AB Prostate cancer is the second most common cause of death from cancer in U.S. men, and advanced, hormone-refractory disease is characterized by painful osteoblastic **bone metastases**. **Endothelin-1**, more commonly known as a potent vasoconstrictor, is a normal ejaculate protein that also stimulates osteoblasts. We show here that plasma immunoreactive endothelin concns. are significantly elevated in men with metastatic prostate cancer and that every human prostate cancer cell line tested produces **endothelin -1** mRNA and secretes immunoreactive endothelin. Exogenous **endothelin-1** is a prostate cancer mitogen in vitro and increases alkaline phosphatase activity in new bone formation, indicating that ectopic **endothelin-1** may be a mediator of the osteoblastic response to bone to metastatic prostate cancer.

L8 ANSWER 2 OF 10 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
AN 1999:29244499 BIOTECHNO
TI Osteomimetic properties of prostate cancer cells: A hypothesis supporting the predilection of prostate cancer metastasis and growth in the bone environment
AU Koeneman K.S.; Yeung F.; Chung L.W.K.
CS Dr. K.S. Koeneman, Molec. Urology/Therapeutics Program, Department of Urology, Univ. of Virginia Hlth. Sci. Center, Charlottesville, VA 22908, United States.
SO Prostate, **(01 JUN 1999)**, 39/4 (246-261), 153 reference(s)
CODEN: PRSTDS ISSN: 0270-4137
DT Journal; Article
CY United States
LA English
SL English
AB BACKGROUND. Unlike most other malignancies, prostate cancer metastasizes preferentially to the skeleton and elicits osteoblastic reactions. METHODS. We present a hypothesis, based upon results obtained from our laboratory and others, on the nature of progression of prostate cancer cells and their predilection to growth and metastasis in the bone microenvironment. We propose the hypothesis that osseous metastatic prostate cancer cells must be osteomimetic in order to metastasize, grow,

and survive in the skeleton. The reciprocal interaction between prostate cancer and bone stromal growth factors, including basic fibroblast growth factor (bFGF), hepatocyte growth factor/scatter factor (HGF/SF), and especially the insulin growth factor (IGF) axis initiates bone tropism, and is enhanced by prostate secreted **endothelin-1** (ET-1) and urokinase-type plasminogen activator (uPA). Growth factors and peptides that have differentiating activity, such as transforming growth factor beta (TGF-β), parathyroid hormone-related protein (PTH-rp), and the bone morphogenetic proteins (BMPs), can shift local homeostasis to produce the characteristic blastic phenotype, via interaction with prostate- secreted human kalikrein 2 (hK2), and prostate-specific antigen (PSA). This proposal asserts that altering the expression of certain critical transcription factors, such as Cbfa and MSX in prostate cancer cells, which presumably are under the inductive influences of prostate or bone stromal cells, can confer profiles of gene expression, such as osteopontin (OPN), osteocalcin (OC), and bone sialoprotein (BSP), that mimic that of osteoblasts. RESULTS AND CONCLUSIONS. Elucidation of common proteins, presumably driven by the same promoters, expressed by both prostate cancer and bone stromal cells, could result in the development of novel preventive and therapeutic strategies for the treatment of prostate cancer skeletal metastasis. Agents developed using these strategies could have the potential advantage of interfering with growth and enhancing apoptosis in both prostate cancer and bone stromal compartments. The selective application of gene therapy strategy, driven by tissue-specific and tumor-restricted promoters for the safe delivery and expression of therapeutic genes in experimental models of prostate cancer metastasis, is discussed.

L8 ANSWER 3 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:184546 BIOSIS
DN PREV200100184546
TI Osteoblastic **bone metastases**: Tumor-produced **endothelin-1** mediates new bone formation via the **endothelin A receptor**.
AU Yin, J. J. [Reprint author]; Grubbs, B. G.; Cui, Y.; Wu-Wong, J. R.; Wessale, J.; Padley, R.; Guise, T. A.
CS University of Texas Health Science Center at San Antonio, San Antonio, TX, USA
SO Cancer, (June 15, 2000) Vol. 88, No. 12, pp. 3093-3094. print.
Meeting Info.: Second North American Symposium on Skeletal Complications of Malignancy. Montreal, Canada. October 15-16, 1999.
CODEN: CANCAR. ISSN: 0008-543X.
DT Conference; (Meeting)
Conference; (Meeting Paper)
LA English
ED Entered STN: 11 Apr 2001
Last Updated on STN: 18 Feb 2002

L8 ANSWER 4 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2000:416086 BIOSIS
DN PREV200000416086
TI **Endothelin A receptor** blockade inhibits osteoblastic metastases.
AU Yin, J. J. [Reprint author]; Grubbs, B. G. [Reprint author]; Cui, Y. [Reprint author]; Wu-Wong, J. R.; Wessale, J.; Padley, R. J.; Guise, T. A. [Reprint author]
CS Medicine/Endocrinology, University of Texas Health Science Center, San Antonio, TX, USA
SO Journal of Bone and Mineral Research, (September, 2000) Vol. 15, No. Suppl. 1, pp. S201. print.
Meeting Info.: Twenty-Second Annual Meeting of the American Society for Bone and Mineral Research. Toronto, Ontario, Canada. September 22-26,

2000. American Society for Bone and Mineral Research.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Sep 2000
Last Updated on STN: 8 Jan 2002

L8 ANSWER 5 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1999:441578 BIOSIS
DN PREV199900441578
TI Osteoblastic **bone metastases**: Tumor-produced **endothelin-1** mediates new bone formation via the **endothelin A receptor.**
AU Yin, J. J. [Reprint author]; Grubbs, B. G. [Reprint author]; Cui, Y. [Reprint author]; Wu-Wong, J. R.; Wessale, J.; Padley, R.; Guise, T. A. [Reprint author]
CS Medicine, Univ. TX Hlth. Sci. Ctr., San Antonio, TX, USA
SO Journal of Bone and Mineral Research, (Sept., 1999) Vol. 14, No. SUPPL. 1, pp. S289. print.
Meeting Info.: Twenty-First Annual Meeting of the American Society for Bone and Mineral Research. St. Louis, Missouri, USA. September 30-October 4, 1999. American Society for Bone and Mineral Research.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 18 Oct 1999
Last Updated on STN: 3 May 2000

L8 ANSWER 6 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2001034106 EMBASE
TI Bone morphogenetic protein-6: Potential mediator of osteoblastic metastases in prostate cancer.
AU Thomas B.G.; Hamdy F.C.
CS F.C. Hamdy, Section of Urology, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, United Kingdom
SO Prostate Cancer and Prostatic Diseases, (2000) 3/4 (283-285).
Refs: 10
ISSN: 1365-7852 CODEN: PCPDFW
CY United Kingdom
DT Journal; Article
FS 016 Cancer
028 Urology and Nephrology
029 Clinical Biochemistry
LA English
SL English
AB The mechanisms by which prostate cancer metastasizes to bone with a strong osteoblastic reaction remain poorly understood. Several factors have been previously implicated, including transforming growth factor-β, fibroblast growth factors, **endothelin-1** and bone morphogenetic proteins (BMPs). BMP-6 expression has been shown exclusively in the malignant epithelial cells of prostate cancers that have metastasized, but not in organ confined disease. Expression of BMP-6 in radical prostatectomy specimens has been shown to correlate with increased recurrence rates and decreased survival. This article presents the results of work by the authors' group in this field and a current literature review.

L8 ANSWER 7 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1999437181 EMBASE

TI Overview: Hormone refractory prostate cancer.
AU Crawford E.D.; Rosenblum M.; Ziada A.M.; Lange P.H.
CS Dr. E.D. Crawford, Univ. of Colorado Health Sci. Center, Box C-324, 4200 East Ninth Avenue, Denver, CO 80262, United States
SO Urology, (1999) 54/6 SUPPL. 1 (1-7).
Refs: 38
ISSN: 0090-4295 CODEN: URGYAZ
PUI S 0090-4295(99)00447-1
CY United States
DT Journal; General Review
FS 016 Cancer
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English

L8 ANSWER 8 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1999094133 EMBASE
TI Cancer and bone.
AU Guise T.A.; Mundy G.R.
CS Dr. T.A. Guise, Division of Endocrinology, Department of Medicine, Univ. of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284-7877, United States. guise@uthscsa.edu
SO Endocrine Reviews, (1998) 19/1 (18-54).
Refs: 475
ISSN: 0163-769X CODEN: ERVIDP
CY United States
DT Journal; General Review
FS 003 Endocrinology
005 General Pathology and Pathological Anatomy
016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
LA English

L8 ANSWER 9 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1998098268 EMBASE
TI The molecular biology of prostate cancer morbidity and mortality: Accelerated death from ejaculate poisoning?.
AU Chou E.; Simons J.W.
CS Dr. J.W. Simons, Johns Hopkins Oncology Center, James Buchanan Brady Urol. Institute, Johns Hopkins Hospital, 600 N. Wolfe Street, Baltimore, MD 21287-2411, United States
SO Urologic Oncology, (1997) 3/3 (79-84).
Refs: 36
ISSN: 1078-1439 CODEN: URONEC
PUI S 1078-1439(97)00041-0
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
016 Cancer
028 Urology and Nephrology
029 Clinical Biochemistry
LA English
SL English
AB The molecular biology of host-tumor interactions unique to human prostate cancer that cause patient morbidity are poorly understood despite the prevalence of this neoplasm. Little is known fundamentally about prostate-specific exocrine gene products secreted by metastatic prostate carcinoma cells at metastatic sites that cause diffuse bone pain, immunosuppression, anemia, cachexia, and other clinical signs of advanced prostate cancer. Growing evidence supports the presence of androgen-

regulated exocrine gene products as independent mediators of prostate cancer morbidity. The experimental and clinical implications of a hypothesis that prostate-specific exocrine genes cause patient morbidity are discussed.

L8 ANSWER 10 OF 10 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1995-45609 DRUGU T S
TI Plasma **endothelin-1** as a marker for doxorubicin cardiotoxicity.
AU Yamashita J; Ogawa M; Shirakusa T
CS Univ.Fukuoka; Univ.Kumamoto
LO Fukuoka; Kumamoto, Jap.
SO Int.J.Cancer (62, No. 5, 542-47, 1995) 4 Fig. 2 Tab. 35 Ref.
CODEN: IJCNAW ISSN: 0020-7136
AV Department of Surgery II, Fukuoka University School of Medicine, Nanakuma 7-45-1, Jonan, Fukuoka 814-01, Japan.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 1995-45609 DRUGU T S
AB In a prospective study of 30 patients with breast cancer (23) or small-cell lung cancer (7) treated with doxorubicin (DR), plasma concentrations of endothelin (ET)-1 increased progressively in 5 cases, not related to cumulative DR dose, and 2/5 developed clinical CHF. Other medications included tamoxifen, 5-fluorouracil, cyclophosphamide, medroxyprogesterone- acetate, 5'-doxifluridine, cisplatin, vincristine and etoposide. Serial measurements of plasma ANF, fractional shortening (FS) studied by M-mode echocardiography, and LV ejection fraction (LVEF) showed no abnormalities until the development of CHF. Patients who did not develop CHF showed no appreciable change in plasma ET-1 or other markers. The results suggest that plasma ET-1 may be useful for predicting the risk of DR-induced cardiotoxicity.
ABEX Methods 30 Consecutive Japanese patients (aged 35-70 yr, mean 55 yr, 6 men) scheduled to receive DR were monitored by ECG and M-mode echocardiography, and blood analysis for DR, ET-1 (by RIA and HPLC) and ANF (by RIA). Results Plasma ET-1 levels rose progressively in 5/30 (3 breast cancer and 2 small-cell lung cancer) patients during DR treatment. 25 Patients given cumulative DR doses of 400-660 mg/sq.m showed no appreciable change in plasma levels of ET-1 or ANF, or in the FS or LVEF. 2/5 Patients with progressive rises in ET-1 developed clinical CHF. 1 Of these was a 52-yr-old woman with lung and **bone metastases** from breast cancer, treated with DR, 5-fluorouracil and cyclophosphamide; she had plasma ET-1 rising from 2.2 to 7.7 pg/ml at 400 mg/sq.m DR, and developed clinical CHF after 2 additional courses of 50 mg/sq.m DR. Baseline and serial FS and LVEF had shown no abnormality until she developed CHF. CHF resolved with medical therapy after stopping DR. In the other case, a 54-yr-old man with extensive small-cell lung cancer treated with DR, vincristine and cyclophosphamide, had shown ET-1 rise from 3.1 to 10 pg/ml after 420 mg/sq.m DR, but no change in FS or LVEF; he developed signs of CHF after the next DR dose (60 mg/sq.m), and improved after stopping DR and treatment with diuretics + fluid restriction. 3 Patients had increases in plasma ET-1 from 2.5 to 7, 2.6 to 8.2 and 2 to 6.9 pg/ml after cumulative 550, 450 and 450 mg/sq.m DR, respectively, then stopped DR and did not develop CHF. (W103/AE)

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